REMARKS

Claim 1 has been amended, along with claim 26 and 32, to make even more clear that at least some of the active is in the granules and a filler (diluent) is in the granules as well. Therefore, in answer to the Examiner's question in objection 2, at least some of the drug is in the granules and at least a filler from the rest of the composition is in the granules too. Basis for amendment is found on page 11, lines 21-22, page 7, lines 23-24, and page 8, lines 16-19 of the specification.

Other amendments have their bases as follows:

-amended claim 14, page 9, lines 4-9 of the specification,

-amended claim 18, page 8, lines 26-32 of the specification,

-amended claim 19, page 8 lines 34-40 of the specification,

-amended claim 23, page 10, lines 1-8 of the specification,

-amended claim 27, page 9, lines 11-13 of the specification,

-amended claims 28, 29, 49, 50, page 11, lines 21-23 of the specification,

-amended claim 38, page 8, lines 34-36 of the specification, and

-amended claims 40 and 51, page 9, lines 33-37 of the specification.

Applicants respectfully traverse the Examiner's objection in paragraph 4. The insoluble-to-slightly-soluble calcium/magnesium phosphate, hydrogen phosphate, carbonate or hydrogen carbonate salts in claims 1, 26 and 32 have been specified.

It is argued, contrary to the assertions of the Examiner, that the use of calcium phosphate, calcium hydrogen phosphate, CaCO3, MgCO3 or the other small class of Ca/Mg salts mentioned in claim 1 are not per se obvious to a skilled artisan in view of Gaster (WO 93/18036) together with International Cosmetic Ingredient Dictionary and Handbook (ICIDH).

First, it is not clear that the skilled artisan reading pages 7-8 of Gaster would combine it with ICIDH to fill in the unstated composition details. There is no basis for combination. Second, there are a large number of binding agents given on page 1625 of the cited dictionary and on page 1625 these bulking agents finish at "M", strongly suggesting that there is an even bigger list. On page 1625, only three excipients, calcium carbonate, calcium phosphate and magnesium carbonate appear to meet the criteria claimed in amended claim 1. This is out of 39 bulking agents on page 1625 and presumably just as many again on unseen page 1626.

There is no direction for extrapolation to the choice of three out of the numerous excipients (about 70 -80). The PTO has, therefore, not met its burden of demonstrating per se obviousness.

On technical effects, with respect to claim 1, CaHPO4 (i.e. dibasic calcium phosphate, dicalcium phosphate, calcium hydrogen phosphate), when mixed with SB 207266 HCl before granulation and then wet granulated, generally improves the flow properties of the SB 207266 HCl salt, generally composed of small particle size, generally cohesive and generally poorly-flowable, as indicated on pages 2-4 of the specification.

Further, it has been observed in some wet-granulated formulations that Calipharm ™ [which is believed to be fine grade $CaHPO_4$ (dibasic calcium phosphate, calcium hydrogen phosphate), possibly present as the dihydrate], tends to exhibit improved properties – e.g. lower disintegration time and/or higher rate of dissolution – compared to lactose or mannitol fillers. Test formulations wet-granulated with water are thought to contain the following intragranular ingredients: ca. 8.8% w/w SB 207266 HCl, ca. 5% HPMC, ca. 20% microcrystalline cellulose (Avicel PH102), ca. 5% Explotab, and either about 59-60% mannitol or alternatively about 59-60% Calipharm, (plus ca. 2% Mg stearate extragranularly). The stated Calipharm formulation appeared to exhibit a slightly better (i.e. smaller) disintegration time compared with the stated mannitol formulation after compression of the granules + Mg stearate into tablets, when measured after compression at medium–to-high upper punch settings (medium-to-high tablet compression force). In a test wet-granulated formulation, apparently with ca. 22% w/w intragranular SB 207266 HCl, ca. 46% intragranular regular lactose, ca. 5% HPMC, ca. 5% sodium starch glycollate, ca. 20% microcrystalline cellulose, ca. 1% Mg stearate (Avicel PH102), appeared to show a not-wholly-satisfactory granulation process as the mass became "doughy" and malleable and broke down into granules less easily so that the granulation yield was only moderately low, though the resulting lactose-containing granules appeared to compress satisfactorily. The "time to 75% released" for these lactose-containing tablets appear not to be ideal.

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In view of the above remarks, Applicants are of the view that the present claims are allowable. Reconsideration of this application is requested. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned agent at the number below.

Respectfully submitted,

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